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(54) Prosthesis

(57) In our Patent No. 2099702B, we have described and claimed a temporary prosthesis comprising a body of non-toxic material, e.g. a glass, soluble in body fluids over an extended period. The prosthesis provides post-operative support for bone or tissue members. As healing proceeds, the prosthesis slowly dissolves into the body fluids, which obviates the need for surgical removal. The glass thus used is typically a P_2O_5/CaO/Alkali metal oxide, whose dissolution rate can be controlled to the desired value.

The principles of the above Patent have been extended to give glasses which dissolve in water of pH of 6 to 8 at less than 20mg.cm^{-2}h^{-1} at 38°C. Such glasses include P_2O_5 as glass-forming oxide, with one or more of CaO, ZnO, MgO, plus one or both of the additional modifying oxides Na_2O and K_2O. The proportion of P_2O_5 is in the range 28 mole % to 50 mole %, and the proportion of the one or more of CaO, ZnO, MgO is in the range 2 mole % to 47 mole %

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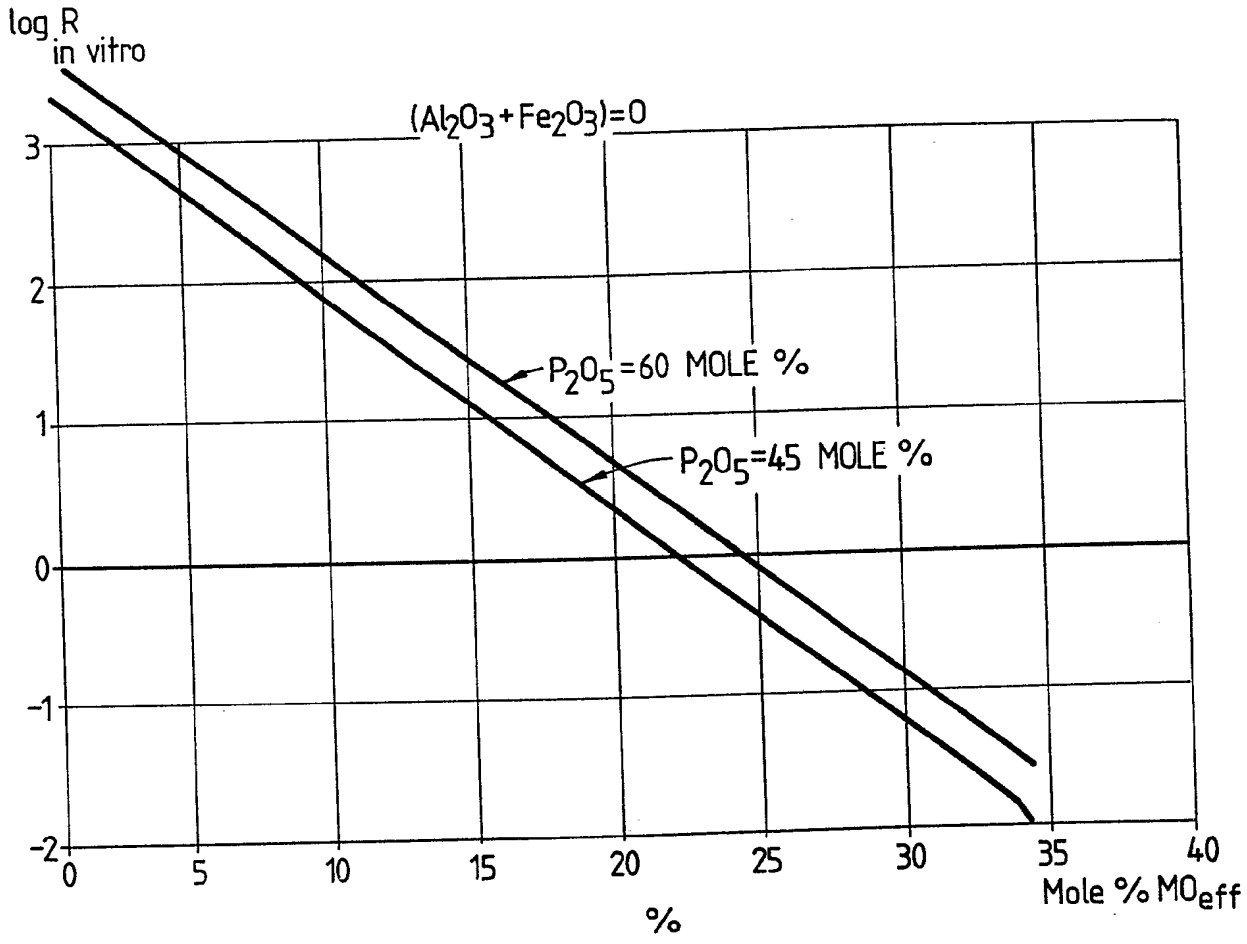
The drawing(s) originally filed was (were) informal and the print here reproduced is taken from a later filed formal copy.

$$\text{I}\quad \log R = \frac{79 - P_2O_5}{10} - 0{\cdot}154(MO)_{eff}$$

$$\text{II}\quad \log R_{(Al_2O_3 + Fe_2O_3)} = \log R - (Al_2O_3 + Fe_2O_3)$$



SPECIFICATION

Prosthesis

This invention relates to water-soluble structural compositions, and especially to water-soluble surgical support structures.

Surgical operations of an orthopaedic nature often involve the use of a temporary structure during the post-operative healing process. The exact nature of the support structure depends on the operation performed, but often the use of such a structure needs another operation to remove it. This involves the patient in further discomfort and risk of infection, and is relatively costly. Further, the "follow-up" operation disturbs healing process and may give rise to medical complications.

In our Patent No. 2099202B we have described and claimed a prosthetic implant which is based on the use of controlled release glass techniques, and claim 1 of this Patent reads as follows:

"A temporary prosthesis for providing post-operative support of skeletal or tissue members, the prosthesis including a rigid body wholly or partially comprising a non-toxic glass composition soluble in body fluids, and wherein the dissolution rate of the material is such that the prosthesis retains its supportive properties for a period sufficient for the skeletal or tissue member to be become self-supporting."

The glass compositions described in the above-mentioned Patent Specification are based on the use of phosphorous pentoxide (P_2O_5) as the principle glass-forming oxide, and oxides selected from Na_2O, K_2O, CaO, MgO and ZnO as the principle glass-modifying oxides. These oxides are bio-compatible in that they can be implanted in animals including man, either sub-cutaneously or intraperitoneally, in soft tissue or in bone, without producing significant local reaction and without any contra-indications relating to long-term effects.

The above-quoted Patent Specfication also discloses that by selection of the ratios of the constituent oxides, it is possible to prepare such glasses which when implanted dissolve completely, leaving no residue. That Specification also discloses that the rate of solution of such glasses is increased as the proportion of the alkali metal oxide is increased, and decreases as the proportion of the Group II metal oxide is increased.

The present invention has as its object the extension of the principles on which the above-mentioned Patent Specification is based.

According to the invention, there is provided a non-toxic water-soluble glass which dissolves in water with a pH of 6 to 8 at a rate less than $20mg.cm^{-2}h^{-1}$ at 38°C, including one or more of the glass-modifying oxides CaO, ZnO, MgO, together with P_2O_5 as the glass-forming oxide, and one or both of the additional glass-modifying oxides Na_2O and K_2O, and wherein the constituent oxides are present in such proportions that the proportion of P_2O_5 is greater than 28 mole % and less than 50 mole %, and the proportion of said one or more of CaO, MgO and ZnO is greater than 2 mole % and less than 47 mole %.

Thus the compositions specified herein constitute a specific selection of compositions, all of which would fall within some at least of the claims of the above-quoted Patent Specification.

Embodiments of the invention will now be described with reference to the accompanying drawing, which shows curves used to explain certain aspects of the invention.

We have now found that particular ranges of glass composition are to be preferred for particular applications, and that the solution rate can be selected by adjusting the relative proportions of the constituent oxides. In the following description and in certain of the claims, compositions are expressed as mole % of the oxides.

The solution rate is here expressed as $R_{in\ vitro}$ which is defined as milligrams of glass dissolved per square centimetre of glass per hour in flowing water of pH of approximately 7 at 38°C.

This invention particularly relates to the use of a phosphate-based glass as a structural material for use in animal or human surgery, although the materials are not limited to such applications.

The surgical applications of the glasses described herein can for convenience be divided into three groups:

(1) monolithic, homogeneous, glass blocks, plates, rods, fibres, etc.
(2) foamed glass plates, rods, granules.
(3) glass fibres, solid or hollow.

When the glass is used in surgery, it is normally desirable for the glass to dissolve completely in a time not less than the time needed for the surgical incision to heal, and not greater than the time needed for new tissue to grow and replace the temporary structure provided by the glass. Thus the required total dissolution time for the device is normally not less than one week and not more than ten weeks.

We now consider each of the above cases to define the range of values of thickness needed, and hence the range of preferred compositions of the glass. Usually in practice the device has dimensional limits as follows:

(1) the maximum thickness t_m of the monolithic glass is $0.5cm > t_m > 0.1cm$.

(2) the maximum dimensions t_f of the foamed glass units is normally $1cm > t_f > 0.11cm$. Total dissolution occurs by sequential dissolution of the walls of the cavities and the cumulative thickness of glass to be dissolved is between 0.8 and 0.4 × t_f. That is, the effective glass thickness t_{fe} is given by $0.8cm > t_{fe} > 0.4cm$.

(3) the fibre thickness or capillary wall thickness t_c is given by $0.02cm > t_c > 0.001cm$.

As the glass normally dissolves from two "faces", the actual thickness t_d to be dissolved is half the above values. Thus we have:

(1) $0.25cm > t_{d1} > 0.05cm$
(2) $0.4cm > t_{d2} > 0.02cm$
(3) $0.01cm > t_{d3} > 0.0005cm$

The thickness of the layer of glass removed per unit time is given by:

$$R_{th} = R_{in\ vitro} \times \frac{(24 \times 7)}{1000p}\ cm/week$$

where p is the density of glass, which is approximately 2.5gm.cm^{-3}.

From the above it follows that the extreme range of values of solution rates needed for each of the three classes of applications, assuming that the total solution time lies between a minimum of one week and a maximum of ten weeks, are:

R_1 = 3.7 to 0.06mg.cm^{-2}.h^{-1}

R_2 = 6 to 0.02mg.cm^{-2}.h^{-1}

R_3 = 0.1 to 0.0007mg.cm^{-2}.h^{-1}

We have found that the actual rate of solution of these glasses when implanted in the animal is up to four times slower than the $_{in\ vitro}$ rate and it is therefore necessary to make provision for glasses with a value of $R_{in\ vitro}$ of up to 15mg.cm^{-2}.h^{-1}.

We have found that glasses to meet the above requirements can be made as indicated in the following tables.

TABLE 1

BATCH WT.g

	NaH_2PO_4	$CaHPO_4$	$Zn_3(PO_4)_2.2.3H_2O$	$3MgCO_3.Mg(OH)_2.3H_2O$	Na_2CO_3	P_2O5	$Al(OH)_3.\times H_2O$
1	45.6	7.5	4.4	—	0.5	—	
2	42.71	16.56	—	—	14.23	—	
3	46.8	7.5	—	2.7	0.3	—	
4	40.37	19.36	—	—	13.19	—	
5	45.6	5.4	—	4.1	—	2.5	
6	34.5	18.3	—	—	—	3.64	
7	44.4	6.1	—	3.9	—	1.1	0.6
8	30.1	15.2	—	1.3	—	1.5	1.1

	Melt Temp °C	*Melt Time Min.*	*Anneal °C*	*R mg.cm^{-2}.h^{-1}*	*Wt. loss on melting, g*
1	1150	20	350	12.0	8.7
2	1140	20	300	4.6	14.4
3	1100	15	350	1.6	9.9
4	1140	20	350	1.8	13.8
5	1100	15	350	0.6	10.4
6	1150	20	350	0.2	7.1
7	1200	20	350	0.03	9.0
8	1200	20	350	0.0008	6.3

Preparation of glass

The batch constituents were mixed as dry powders and melted at the indicated temperatures and times in a platinum crucible, in an electric resistance furnace in air. It was then cast into 4mm cylindrical rods in a steel mould, and cooled from the annealing temperature indicated at a constant cooling rate over 15 hours. R was measured at 38°C in distilled water flowing at 0.06 litres/hour.

The composition of the glasses for application class 1 and 2 above (20 > R > 0.06), can be selected using the accompanying graph, or equation 1 quoted on that graph.

For glasses for class 3 applications, it may be necessary to include either Al_2O_3 or Fe_2O_3 in the glass composition, and the amount of either of these oxides can be selected using the graph, or equation I plus equation II, which defines the reduction in solution rate R produced by the addition of a given amount of (Al_2O_3 + Fe_2O_3).

Depending on the specific application for which the glass is intended, certain other glass-modifying oxides may be included in the mix. These oxides include Ag_2O, SrO, FeO, CuO, TiO_2 and ZrO_2, of which not more than 5 mole % is used. Similarly, up to 5 mole % of one or both of colloidal Au^0 and Pt^0 may be present. Finally, up to 5 mole % of the glass former P_2O_5 may be replaced by SiO_2 or one or more of the ions as radicals F^-, I^-, SO_4^{--}, SeO_3^{--}, or BO_3^{--}.

CLAIMS

1. A non-toxic water-soluble glass which dissolves in water with a pH of 6 to 8 at a rate less than

$20mg.cm^{-2}h^{-1}$ at 38°C, including one or more of the glass-modifying oxides CaO, ZnO, MgO, together with P_2O_5 as the glass-forming oxide, and one or both of the additional glass-modifying oxides Na_2O and k_2O, and wherein the constituent oxides are present in such proportions that the proportion of P_2O_5 is greater than 28 mole % and less than 50 mole %, and the proportion of said one or more of CaO, MgO and ZnO is greater than 2 mole % and less than 47 mole %.

2. A glass as claimed in claim 1, and which includes not more than 5 mole % of $(Al_2O_3 + Fe_2O_3)$.

3. A glass as claimed in claim 1 or 2, in which not more than 5 mole % of the glass-forming oxide P_2O_5 is replaced by one or more of the ions or radicals F^-, I^-, SO_4^{--}, SeO_3^{--}, or BO_3^{--}.

4. A glass as claimed in claim 1, 2 or 3, and in which not more than 5 mole % of the glass-forming oxide P_2O_5 are replaced by one or more of the oxides SrO, Ag_2O, FeO, CuO, TiO_2 and ZrO_2.

5. A glass as claimed in claim 1, 2, 3 or 4, and which contains not more than 5 mole % of one or both of colloidal Au^0 and Pt^0.

6. A glass as claimed in any preceding claim, whose solution rate R_{th} is defined as thickness in millimetres of the layer of annealed glass dissolved in one week when the glass is immersed in water of pH 6 to 8 at 38°C, wherein R_{th} is not more than 8mm per week and not less than 5×10^{-4}cm per week, and wherein the glass comprises:

(i) more than 2 mole % MO_{CFF} and less than 45 mole % MO_{CFF}, where MO_{CFF} is derived from the formula $M_{CFF} = CaO + 1.6\,MgO + 0.7\,ZnO$; and

(ii) more than 28 mole % P_2O_5 and less than 50 mole % P_2O_5, the P_2O_5 being sufficient to produce a glass which does not readily devitrify.

7. A glass as claimed in claim 6, and which also contains a total of less than 5 mole % of the oxides Al_2O_3, Fe_2O_3.

8. A glass as claimed in claim 6 or 7, in which the composite is selected to give a chosen solution by the use of the graph shown in the accompanying drawing.

9. A biocompatible resorbable component for use in surgery and which mainly comprises a glass as claimed in any one of claims 1 to 8.

10. A component as claimed in claim 9, in which the glass is in the form of a moulded unit, a tube, a rod, a fibre or bundle of fibres, a capillary or bundle of capillaries, a cloth or tape prepared from fibre, a foamed glass preform or a sintered glass preform.

11. An implantable component as claimed in claim 9 or 10.

12. A non-toxic water soluble glass, substantially as hereinabove described.

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